REMARKS

This submission is in response to the non-final Office Action electronically mailed on February 24, 2009. Claims 1, 2, 4-6, 10, 11 and 20-22 have been amended. Claims 1 and 21 have been amended to recite a weight ratio of morphine:chitosan from about 5:1 to about 15:1. Support for this amendment can be found, for example, at page 7, line 4 and page 14, lines 14-18 of the Application as filed. Claims 1, 2, 4-6, 20-22 have also been amended to recite morphine, instead of morphine base monohydrate. Support for this amendment can be found, for example in the original claims and page 4, line 5 of the Application as filed. The preamble to claim 21 has been amended so that it is consistent with claims 1 and 26. Claims 10 and 11 have been amended to recite standard *Markush* language.

Claims 24-33 have been added. Claims 24 and 25 recite weight ratios of morphine:chitosan of about 7.5:1 and 15:1, respectively. Support for this amendment can be found, for example, on page 14, lines 14-18 of the Application as filed. Claim 26 essentially tracks claim 21 and includes a recitation regarding the molecular ratio of morphine to the controlled release chitosan polymer being from about 1:1 to about 23,000:1. Support for this amendment can be found, for example, on page 6, line 28 and page 14, line 21 of the Application as filed. Claim 27 recites a molecular ratio of morphine to controlled release chitosan polymer of about 11,500:1. Claim 28 recites a molecular ratio of morphine to controlled release chitosan polymer of about 23,000:1. Support for these amendments can be found, for example, on page 14, line 21 of the Application as filed. Claims 29-32 recite pH ranges from about 3.0 to about 7.0, and from about 4.0 to about 5.0. Support for these amendments can be found, for example, on page 8, line 5 of the Application as filed. Claims 33 and 35 specify that the morphine is morphine mesylate. Support for these amendments can be found, for example, on page 5, line 7 of the Application as filed. Claims 34 and 36 specify that the controlled release chitosan polymer is chitosan, as opposed to a derivative or salt of chitosan (which, in turn, are encompassed by, for example, claims 1, 21, 26). Support for this Amendment can be found, for example, on page 5, lines 21-22 of the Application as filed.

No new matter has been added by these claim amendments.

A. Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-2, 4-17, 21-23 stand rejected as failing to comply with the written description requirement. According to the Examiner, the claims embrace subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the art that the applicants, at the time the Application was filed, had possession of the claimed invention.

Specifically, the Examiner asserts that the specification only provides a description that supports the use of "linear" forms of chitosan that are composed of acetylated and deacetylated D-glucosamine units for transmucosal delivery, not derivative or salt forms. In this regard, the Examiner asserts that one of ordinary skill in the art would not expect the latter two forms of chitosan to have the exact same properties as "linear" chitosan and, hence, be suitable for transmucosal delivery.

Applicants respectfully traverse this rejection for the reasons that follow:

I. To Reject Originally Claimed Subject Matter, The PTO Bears A Heavy Burden

At the outset Applicants wish to note that the phrase "chitosan polymer" was employed in the original set of claims presented for examination and the Application, as filed, provides definitions for and examples of "chitosan polymers," "chitosan salts," and "chitosan derivatives." *See* Specification, pages 5-6. In fact, the Examiner herself acknowledges that the Application contains such disclosure.

As explained in MPEP §2163, there is a strong presumption that an adequate written description of claimed invention is present when the Application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims"). A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See, e.g., In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Examiner, therefore,

must have a reasonable basis to challenge the adequacy of the written description. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97.

More generally, the MPEP instructs that, when rejecting a claim under a theory of lack of written description, the examiner must set forth express findings of fact that:

(A) Identify the claim limitation at issue; and

(B) Establish a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the Application as filed. *See* MPEP §2163 III.A.

Applicants respectfully submit that the Examiner's rejection does not properly comply with the foregoing case law or guidelines. In particular, she has not presented evidence or reasoning that is *sufficient* to support the rejection. At most, she has provided unsupported conjecture.

II. The Specification Enables One Of Ordinary Skill to Structurally Envisage Chitosan Salts and Derivatives And Recognize Their Suitability For Transmucosal Delivery

While the Examiner notes that "a lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process," such concerns are not present here. The Application describes salt and derivative forms of chitosan with sufficient specificity that they can be envisaged by the person of ordinary skill. The Application states that various forms of chitosan may be used when "a greater proportion of the N-acetyl groups [of chitin] have been removed through hydrolysis (deacetylation)." Specification, page 5, lines 28-29. Furthermore, with respect to salt forms of chitosan, the Application identifies seven representative salt species. Specification, page 5, line 31 to page 6, line 1. With respect to derivatives, the Application discloses that such derivatives: a) are "formed by bonding acyl and/or alkyl groups with OH groups, but not the NH_2 groups, of chitosan:" and b) can take the form of esters, ethers and PEG conjugates. Specification, page 6, lines 2-5.

In addition to allowing one of ordinary skill to structurally envisage chitosan salts and derivatives, the Application implicitly illustrates that there is a common core structure shared among the various chitosan species being claimed that unifies them under a common genus, *i.e.*, a deacetylated chitin backbone. Because of this, one of ordinary skill in would recognize that salt and derivative forms of chitosan would be as suitable for transmucosal delivery as "linear" forms, and, in turn, that the Applicants were in possession of this concept. *See Eli Lilly*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (the written description requirement for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure); MPEP § 2163 II.A.3.(a) ("Possession may be shown in many ways . . . An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as the person of ordinary skill in the art would recognize that the inventor had possession of the claimed invention").

III. Conclusion

In view of the foregoing, applicants respectfully submit that the Examiner has not established a *prima facie* case that is consistent with the case law or guidelines discussed above. Moreover, given the description that is provided, the specification adequately illustrates possession of the concept of using a salt or derivative form of chitosan for transmucosal delivery. Because claims 1-2, 4-17, 21-23 are adequately described, Applicants respectfully request that the written description rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

B. Rejections Under 35 U.S.C. § 103

Claims 1-2, 4-17 and 21-23 stand rejected as obvious over U.S. Patent No. 6,387,917 issued to Illum et al. (hereafter "Illum"). The Examiner states that Illum discloses a methane sulfonate salt of morphine and compositions thereof having medicinal uses, particularly for the treatment of pain. According to the Examiner, Illum's preferred composition comprises aqueous solutions in which the methane sulfonate salt is combined with chitosan to provide an increased absorption of the drug.

The Examiner admits that the claims differ from Illum by reciting various concentrations of active ingredients(s). Nevertheless, according to the Examiner, the preparation of various transmucosal compositions having various amounts of the active ingredient and

chitosan polymers is within the level of skill of one of ordinary skill in the art at the time of the invention. Applicants respectfully disagree.

Assuming the Examiner were correct in her assumption that the person of ordinary skill would be motivated to optimize the ratios of morphine to a controlled release chitosan polymer, the Examiner has offered no evidence to substantiate that such optimization would result in arriving at the ratios now claimed.

Moreover, assuming for argument's sake that the person of ordinary skill were motivated to optimize Illum's teachings to arrive at the claimed ratios, that individual would not have appreciated that morphine could be absorbed in a substantially linear fashion. Applicants have surprisingly found that, in the claimed compositions, morphine exhibits substantially linear absorption upon administration. Such absorption: a) provides a controlled increase in therapeutic plasma levels of morphine during the drug's absorption or uptake; and b) reduces the risk of morphine overdose. Specification page 7, lines 8-18.

Hence, any "optimization" that the person of ordinary skill might engage in does not detract from the surprising and unexpected finding that the claimed compositions exhibit a linear form of uptake; nothing in Illum (or the prior art of which the Applicants are aware) teaches or suggests that a composition comprising morphine and chitosan (let alone in the ratios claimed) can exhibit such a result.

Accordingly, Applicants respectfully submit that the claims are not obvious over Illum and request that the rejection be withdrawn.

C. No Waiver

All of Applicants' arguments and amendments are without prejudice or disclaimer. Additionally, Applicants have provided some arguments that undermine the positions taken by the Examiner and, in turn, support the patentability of the claims. Other arguments may exist, and Applicants reserve the right to rely on the same at a later point, if appropriate. To the extent Applicants have not responded to all statements made by the Examiner, their silence should not be construed as any form of acquiescence or preclude them from addressing the same at a later point, if appropriate. The arguments raised by Applicants are sufficient to overcome the Examiner's rejections.

SUMMARY

In light of the above remarks, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections. Applicants further submit that the Application is now in condition for allowance, and they earnestly solicit timely notice of the same. Should the Examiner have any questions, comments or suggestions in furtherance of the prosecution of this Application, the Examiner is invited to contact the attorney of record.

Applicants believe that there are no fees due in association with the filing of this Response, apart from the fee for extension of time. However, should the Commissioner deem that any additional fees are due, including any fees for extensions of time, the Commissioner is authorized to debit Baker Botts L.L.P. Deposit Account No. 02-0383, Order Number 077350.0136, for any underpayment of fees that may be due in association with this filing.

Dated: July 24, 2009

Respectfully submitted,

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